(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization

International Bureau



(43) International Publication Date 27 May 2004 (27.05.2004)

(10) International Publication Number WO 2004/043964 A2

(51) International Patent Classification7:

C07D 489/02

(21) International Application Number:

PCT/US2003/035463

(22) International Filing Date:

5 November 2003 (05.11.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/424,748 60/425,580

8 November 2002 (08.11.2002) US 12 November 2002 (12.11.2002)

- (71) Applicant (for all designated States except US): MALLINCKRODT INC. [US/US]; 675 McDonnell Boulevard, P.O. Box 5840, St. Louis, MO 63134 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): CANTRELL, Gary, L. [US/US]; 509 Lakewood Drive, Troy, IL 62294 (US). HALVACHS, Robert, E. [US/US]; 309 Fredericksburg Drive, Belleville, IL 62223 (US).

5

- (74) Agents: BOONE, Jeffrey, S. et al.; 675 McDonnell Boulevard, P.O. Box 5840, St. Louis, MO 63134 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



(57) Abstract: A process for the preparation of a quaternary derivative of the morphinan alkaloid, the process comprising contacting a tertiary N-substituted morphinan alkaloid with an alkyl halide in an anhydrous solvent system, wherein the solvent system comprises an aprotic dipolar solvent with the aprotic dipolar solvent constituting at least 25 wt% of the solvent system.